Remarks

I. STATUS OF THE CLAIMS AND SUPPORT FOR THE CLAIM AMENDMENTS

Reconsideration of this application is respectfully requested. Claims 1, 2, 20, 24, 30, 31 and 32 have been amended. Upon entry of the amendments, claims 1-3, 5-7, 11-17, 20, 24-27, and 30-42 are pending. Support for amendments to claims 1, 2 and 20 can be found for example, throughout the specification, for example page 5, lines 19-21. Support for the amendments to claim 32 can be found for example, throughout the specification, for example page 20 and in the original claims as filed. Claims 24, 30 and 31 were amended to depend from claim 20, claim 22 having been previously canceled. Consideration and entry of these amendments is respectfully requested.

All amendments and cancellations are made without prejudice or disclaimer. Applicant explicitly retains the right to pursue any deleted subject matter in one or more continuation applications. No new matter has been added by any of the amendments. Moreover, entry of this Amendment will not expand the scope of any pending claim.

Information Disclosure Statement

A Supplemental Information Disclosure Statement is enclosed in compliance with 37 CFR 1.97(c) for the Examiner's consideration.

The Office Action

Claims 1, 2, 16 and 32 stand rejected under 35 U.S.C. § 112, 2nd paragraph as being indefinite.

Claims 1-3, 5-7 and 11-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pouletty (U.S. Patent No. 5,292,641) in view of Tidey et al. (U.S. Patent No. 6,046,013) and further in view of Chang et al. (U.S. Patent No. 5,270,169) and Walter et al. (International Immunology, Vol. 9, p. 451-459 1997) or Baserga et al (U.S. Patent No. 6,218,363).

Claims 20, 24 and 30-42 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pouletty (U.S. Patent No. 5,292,641) in view of Tidey et al. (U.S. Patent No. 6,046,013) and further in view of Chang et al. (U.S. Patent No. 5,270,169) and

Walter et al. (International Immunology, Vol. 9, p. 451-459 1997) or Baserga et al (U.S. Patent No. 6,218,363) as applied to claims 1-3, 5-7 and 11-17 above, and further in view of Boguslaski et al. (U.S. Patent No. 5,420,016).

Claims 25-27 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pouletty (U.S. Patent No. 5,292,641) in view of Tidey et al. (U.S. Patent No. 6,046,013) and further in view of Chang et al. (U.S. Patent No. 5,270,169) and Walter et al. (International Immunology, Vol. 9, p. 451-459 1997) or Baserga et al (U.S. Patent No. 6,218,363) and further in view of Boguslaski et al. (U.S. Patent No. 5,420,016) as applied to claims 1-3, 5-7 ,11-17, 20, 24, and 30-42 above, and further in view of _____ [perhaps the office was citing Luxembourg et al. U.S. Pub. No. 2004/0137617?]. The Office is invited to provide the full Luxembourg citation.

II. REJECTIONS UNDER 35 U.S.C. 112, ¶ 2

Claims 1, 2, 16 and 32 stand rejected under 35 U.S.C. § 112, ¶ 2 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is respectfully traversed.

Claim 16 stands rejected, allegedly as being indefinite for the recitation of "blood-derived sample", alleging the term is vague and indefinite and "no definition provided for the term in the specification and it is unclear what applicant is trying to encompass" (Office Action of May 29, 2009, Item 6, p. 3). The term "blood-derived sample" appears in the specification, at least at, for example, page 16, lines 17-21 and page 20, lines 27-31. One of skill in the art would understand the term to refer to blood products derived from whole blood, e.g., plasma, purified plasma, serum, whole cells, packed cells, platelets, etc. Thus, the term "blood-derived sample" has well recognized meanings, allowing the reader to infer the meaning of the entire phrase with reasonable confidence (*MPEP* 2173.02). Therefore, the meets and bounds of claim 16 can be determined by one of skill in the art both by looking to the specification and by having a command of the English language. Applicants respectfully request that the rejection of claim 16 under 35 U.S.C. § 112, 2nd paragraph be withdrawn

Claim 32 stands rejected, allegedly as being indefinite for the recitation of (i) "the one or more recombinant HLA molecules", alleging "there is insufficient antecedent

basis for this limitation, (ii) "the alleles of the one or more recombinant HLA molecules are selected from those listed in Table 4" as the claim relies on "external material… and incorporation into claims by express reference to the specification is not permitted (Ex parte Fressola, 27 USPQ2d 1608)" and (iii) in claim 32, line 2, allegedly reciting improper Markush language when reciting, "recombinant HLA molecules are selected from" as the claims "improperly defines it as such" (Office Action of May 29, 2009, Item 6, p. 3). Claim 32 depends from "claim 1 or 2" and thus includes all the limitation of claims 1 or 2.

As amended claim 32 recites, "The method of claim 1 or 2 wherein the alleles of the ~~one or more~~ recombinant HLA molecules are selected from the group consisting of: [the contents of Table 4 now appears in claim 32]_ ~~those listed in Table 4~~." There is no longer a lack of antecedent basis for "the one or more". Table 4's contents are added to claim 32. Finally, the improper Markush language has been corrected. The Office has not specifically recited a ground of rejection under 35 U.S.C. § 112, 2nd paragraph for claims 1 and 2. Applicants respectfully request that the rejection of claims 1, 2 and 32 under 35 U.S.C. § 112, 2nd paragraph be withdrawn.

III. REJECTIONS UNDER 35 U.S.C. 103(a)

1. Rejection of Claims 1-3, 5-7 and 11-17 under 35 U.S.C. § 103(a) as being unpatentable over Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. or Baserga et al.

Claims 1-3, 5-7 and 11-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Pouletty (U.S. Patent No. 5,292,641) in view of Tidey et al. (U.S. Patent No. 6,046,013) and further in view of Chang et al. (U.S. Patent No. 5,270,169) and Walter et al. (International Immunology, Vol. 9, p. 451-459 1997) or Baserga et al (U.S. Patent No. 6,218,363). Applicants respectfully disagree and traverse this rejection as indicated below.

Claims 1 and 2 has been amended to include recitation of, "…wherein antibodies directed to each allele, if present in the sample, are separately detected and identified in less than three hours." Claims 3, 5-7 and 11-17 are dependent either directly or indirectly upon amended claims 1 or 2 and include all the limitations thereof. Amended claims 1

and 2 are directed to methods of detecting the presence of one or more allele specific anti-Major Histocompatability Complex (MHC) antibodies (claim 1) or one or more allele specific anti-Human Leukocyte Antigen (HLA) antibodies (claim 2) in a body fluid sample by contacting the body fluid with *recombinant* MHC molecules (claim 1) or *recombinant* HLA molecules (claim 2) immobilized to discrete sites of a solid support <u>in less than three hours</u>.

After reading Claims 1 and 2, as discussed above, one of skill in the art would conclude that Pouletty et al. does not teach or suggest the instantly claimed method for detecting the presence of anti-MHC or anti-HLA antibodies using *recombinant* MHC or HLA molecules or recombinant molecules immobilized at separate/discrete sites on a solid support. Tidey et al. also fails to teach the use of recombinant MHC or HLA molecules among other differentiators. The methods of Pouletty and Tidey necessarily exceed three hours. Thus, Pouletty et al. does not teach or suggest the instantly claimed method. Likewise, Tidey et al. does not teach or suggest the instantly claimed method. As such, Pouletty et al. in view of Tidey et al. does not teach each and every element of claims 1-3, 5-7 and 11-17.

Chang et al. does not cure the deficiencies of Pouletty et al. in view of Tidey et al. Chang et al. does not teach a method for detecting anti-HLA antibodies in less than three hours. At most, Chang et al. illustrate a method for detecting anti-HLA antibodies and that synthetic HLA antigens can mimic HLA antigens for detection of specific antibodies in a biological sample. Each of Pouletty et al. (col. 6, ¶ 2), Tidey et al. (col . 8) and Chang et al. ("Experimental" col. 5 bridging Col. 6) require an overnight incubation with antigen or antibody to secure binding of the material to the solid support. The claimed methods can be performed in just 30 minutes for immobilizing the HLA monomer (molecule) to the solid support (see Example 1). Thus, the claimed methods' time to results is under three hours while the methods of Pouletty et al., Tidey et al. and Chang et al. range from around 12-15 hours to over 3 days (Tidey et al.). Applicants respectfully maintain that Chang et al. does not teach every element of claims 1 or 2. As such, Chang et al. cannot teach each and every element of claims 1-3, 5-7 and 11-17.

Neither Walter et al. nor Baserga et al. cure the deficiencies of Pouletty et al. in view of Tidey et al. As with Chang et al., neither Walter et al. nor Baserga et al. teach a

method for detecting anti-HLA antibodies in less than three hours. At most, Walter et al. disclose the use of recombinant HLA molecules to detect antibodies in a sample and Baserga et al. disclose production of MHC or HLA Class I molecules by recombinant DNA techniques. Therefore, Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. or Baserga et al. fail to teach all of the claim limitations. Therefore, the claim limitations are neither taught nor suggested by the prior art, M.P.E.P. § 2143.03. Thus, a *prima facie* case of obviousness has not been made against the pending claims. Accordingly, it is respectfully requested that the rejection under 35 U.S.C. § 103(a) of claims 1-3, 5-7 and 11-17 be withdrawn.

2. Rejection of Claims 20, 24 and 30-42 under 35 U.S.C. § 103(a) as being unpatentable over Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al as applied to claims 1-3, 5-7 and 11-17 above, and further in view of Boguslaski et al. (U.S. Patent No. 5,420,016).

Claims 20, 24 and 30-42 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. as applied to claims 1-3, 5-7 and 11-17 above, and further in view of Boguslaski et al.. Applicants respectfully disagree and traverse this rejection as indicated below.

Claims 24, 30 and 31 are dependent upon claim 20. Claims 32-42 are dependent upon amended claims 1or 2 and include all the limitations thereof. It appears that this rejection is based on the disclosure by Boguslaski et al. of assembling various system components into a test kit (Office Action of May 29, 2009, page 9). Claim 20 is directed to [a] kit comprising at least the following components: a) a solid support comprising discrete sites, each of said sites comprising recombinant MHC molecules representing a single MHC allele to allow separate detection and identification of anti-MHC antibodies binding thereto; and b) a moiety capable of direct or indirect detection of anti-MHC-antibodies bound to said recombinant MHC molecules; wherein said detection occurs in less than 3 hours.

Amended claims 1 and 2 are directed to methods of detecting the presence of one or more allele specific anti-Major Histocompatability Complex (MHC) antibodies (claim

1) or one or more allele specific anti-Human Leukocyte Antigen (HLA) antibodies (claim 2) in a body fluid sample by contacting the body fluid with *recombinant* MHC molecules (claim 1) or *recombinant* HLA molecules (claim 2) immobilized to discrete sites of a solid support and said antibodies are detected and identified in less than three hours." .

As discussed above, neither Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al as applied to claims 1-3, 5-7 and 11-17 above, teach or suggest the instantly claimed method. Nowhere in Pouletty, is there any suggestion to detect anti-MHC or anti-HLA antibodies using recombinant MHC or HLA molecules in a body fluid. Further, the method of Pouletty is in excess of 12 to 15 hours before a result is detected. As amended the time to results for the claimed method is less than about three hours. Thus, Pouletty does not teach or suggest the instantly claimed method. Tidey et al. fails to make up for the deficiencies of Pouletty as discussed *supra*. Moreover, Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. as applied to claims 1-3, 5-7 and 11-17 above do not teach or suggest the instantly claimed method as discussed *supra*. As such, Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. as applied to claims 1-3, 5-7 and 11-17 above cannot teach each and every element of claims 20, 24 and 30-42.

And Boguslaski et al. does not cure the deficiencies of Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. Boguslaski et al. does not teach a method or a kit wherein the detection occurs in less than three hours. At most, Boguslaski et al. discloses assembling various systems components into a test kit. Boguslaski et al. et al. does not teach a recombinant MHC or HLA molecule. Applicants respectfully maintain that Boguslaski et al. et al. does not teach every element of claims 1 or 2 or claim 20. As such, Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. and Boguslaski et al. cannot teach each and every element of dependent claims 24 and 30-42.

Therefore, all of the claim limitations are neither taught nor suggested by the prior art. M.P.E.P. § 2143.03. Thus, a *prima facie* case of obviousness has not been made against the pending claims. Accordingly, it is respectfully requested that the rejection under 35 U.S.C. § 103(a) of claims 20, 24 and 30-42 be withdrawn.

3. Rejection of Claims 25-27 under 35 U.S.C. § 103(a) as being unpatentable over Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. or Baserga et al. and further in view of Boguslaski et al. as applied to claims 1-3, 5-7 ,11-17, 20, 24, and 30-42 above, and further in view of [Luxembourg et al. U.S. Pub. No. 2004/0137617]

Claims 25-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. and further in view of Boguslaski et al. as applied to claims 1-3, 5-7, 11-17, 20, 24 and 30-42 above, and further in view of [Luxembourg et al. U.S. Pub. No. 2004/0137617]. For the sake of advancing prosecution, Applicants' representative has assumed the Office was referring to the Luxembourg application cited in the Final Office Action dated September 29, 2008. The Office is invited to provide the omitted citation. Applicants respectfully disagree and traverse this rejection as indicated below.

Claims 25-27 are dependent either directly (claim 25) or indirectly (claims 26-27) upon amended claims 1or 2 and includes all the limitations thereof. Amended claims 1 and 2 are directed to methods of detecting the presence of one or more allele specific anti-Major Histocompatability Complex (MHC) antibodies (claim 1) or one or more allele specific anti-Human Leukocyte Antigen (HLA) antibodies (claim 2) in a body fluid sample by contacting the body fluid with *recombinant* MHC molecules (claim 1) or *recombinant* HLA molecules (claim 2) immobilized to discrete sites of a solid support and said antibodies are detected and identified in less than three hours.

As discussed above, neither Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al and further in view of Boguslaski et al. as applied to claims 1-3, 5-7, 11-17, 20, 24 and 30-42 above, teach or suggest the instantly claimed method. Nowhere in Pouletty is there any suggestion to detect anti-MHC or anti-HLA antibodies using recombinant MHC or HLA molecules in a body fluid. Further, the method of Pouletty is in excess of 12 to 15 hours before a result is detected. As amended, the time to results for the claimed method is less than about three hours. Thus, Pouletty does not teach or suggest the instantly claimed method. Tidey et al. fails to make up for the deficiencies of Pouletty as discussed *supra*. Moreover, Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. as applied to

claims 1-3, 5-7, 11-17, 20, 24 and 30-42 above do not teach or suggest the instantly claimed method as discussed *supra*. As such, Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. as applied to claims 1-3, 5-7, 11-17, 20, 24 and 30-42 above cannot teach each and every element of claims 25-27.

And Luxembourg et al. does not cure the deficiencies of Pouletty in view of Tidey et al., and further in view of Chang et al., Walter et al., Baserga et al. and Boguslaski et al. Luxembourg et al. does not teach a method wherein the detection occurs in less than three hours. At most, Luxembourg et al. disclose recombinant MHC molecules that are biotinylated. Luxembourg et al. et al. does not teach a method of detecting and identifying MHC or HLA antibodies in less than three hours. Applicants respectfully maintain that Luxembourg et al. et al. does not teach every element of claims 1 or 2 or claims 25-27. As such, Pouletty in view of Tidey et al., and further in view of Chang et al. and Walter et al. and Baserga et al. and Boguslaski et al. and further in view of Luxembourg et al. cannot teach each and every element of dependent claims 25-27.

Therefore, all of the claim limitations are neither taught nor suggested by the prior art. M.P.E.P. § 2143.03. Thus, a *prima facie* case of obviousness has not been made against the pending claims. Accordingly, it is respectfully requested that the rejection under 35 U.S.C. § 103(a) of claims 25-27 be withdrawn.

CONCLUSIONS

In view of the foregoing, Applicants believe that the application is in condition for allowance and a notice thereof is respectfully solicited. If any issues remain in connection herewith, or a telephone interview would be of assistance in advancing prosecution of the application, the Examiner is respectfully invited to telephone the undersigned to discuss.

Prompt and favorable consideration of this response is respectfully requested.

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